B1 cont'd

the first release phase comprising potassium clavulanate and a first portion of the amoxicillin;

the second release phase comprising a second portion of amoxicillin, which is a pharmaceutically acceptable soluble salt of amoxicillin, and at least one pharmaceutically acceptable organic acid which are admixed in intimate contact at a ratio of from 20:1 to 1:2 (amoxicillin free acid equivalent to organic acid equivalent).

B2

18. (amended). A method according to claim 1 in which the bacterial infection is caused by at least one of the organisms *S. pneumoniae, H. influenzae,* and *M. catarrhalis.*

Please add the following claims:

B3

69. A method according to claim 18 wherein the *S. pneumoniae* are Drug Resistant *S. pneumoniae* and Penicillin Resistant *S. pneumoniae* organisms.

70. A method according to claim 13 wherein the amount of amoxicillin in the first release phase is released upon exposure to an aqueous environment.

71. A method according to claim 13 wherein the ratio of the amoxicillin free acid equivalent to organic acid equivalent in the second release phase is from about 2:1 to about 1:1.2.

72. A method according to claim 13 wherein the ratio of the amoxicillin (amoxicillin free acid equivalent) in the first release phase to the amoxicillin (amoxicillin free acid equivalent) in the second release phase is from about 3:1 to about 1:3.

73. A method according to claim 13 wherein the ratio of the amoxicillin (amoxicillin free acid equivalent) in the first release phase to the amoxicillin (amoxicillin free acid equivalent) in the second release phase is from about 2:1 to about 2:3.

74. A method according to claim 71 wherein the ratio of the amoxicillin (amoxicillin free acid equivalent) in the first release phase to the amoxicillin (amoxicillin free acid equivalent) in the second release phase is from about 2:1 to about 2:3.

75. A method according to claim 13 wherein the ratio of the amoxicillin (amoxicillin free acid equivalent) in the first release phase to the amoxicillin (amoxicillin free acid equivalent) in the second release phase is from about 3:2 to about 1:1.

B3

76. A method according to claim 71 wherein the ratio of the amoxicillin (amoxicillin free acid equivalent) in the first release phase to the amoxicillin (amoxicillin free acid equivalent) in the second release phase is from about 3:2 to about 1:1.

77. A method according to claim 13 wherein the ratio of the amoxicillin (amoxicillin free acid equivalent) in the first release phase to the amoxicillin (amoxicillin free acid equivalent) in the second release phase is about 9:7.

78. A method according to claim 13 wherein the at least one pharmaceutically acceptable organic acid is selected from pharmaceutically acceptable monocarboxylic and polycarboxylic acids having from 2 to 25 carbon atoms, pharmaceutically acceptable monocyclic aryl and polycyclic aryl acids, and pharmaceutically acceptable monohydrogen and dihydrogen metal salts of any of the foregoing multi-valent acids.

79. The method according to claim 13 wherein the at least one pharmaceutically acceptable organic acid is selected from pharmaceutically acceptable monocarboxylic and polycarboxylic acids having from 2 to 10 carbon atoms and an acidic salt of any of the foregoing.

80. The method according to claim 71 wherein the at least one pharmaceutically acceptable organic acid is selected from pharmaceutically acceptable monocarboxylic and polycarboxylic acids having from 2 to 10 carbon atoms and an acidic salt of any of the foregoing.

81. The method according to claim 75 wherein the at least one pharmaceutically acceptable organic acid is selected from pharmaceutically acceptable monocarboxylic and polycarboxylic acids having from 2 to 10 carbon atoms and an acidic salt of any of the foregoing.

82. A method according to claim 13 wherein the at least one pharmaceutically acceptable organic acid is selected from $C_{(2-10)}$ alkyl- and $C_{(2-10)}$ alkenyl- carboxylic acids having one, two, or three carboxylic acid groups, and optionally at least one hydroxy substituent, and optionally at least one -CO group in the carbon chain and an acidic salt of any of the foregoing.

83. A method according to claim 13 wherein the at least one pharmaceutically acceptable organic acid is selected from malonic acid, succinic acid, fumaric acid, maleic acid, adipic acid, lactic acid, levulinic acid, sorbic acid, tartaric acid, maleic acid, ascorbic acid, citric acid, and an acidic salt of any of the foregoing.

84. A method according to claim 71 wherein the at least one pharmaceutically acceptable organic acid is selected from malonic acid, succinic acid, fumaric acid, maleic acid, adipic acid, lactic acid, levulinic acid, sorbic acid, tartaric acid, maleic acid, ascorbic acid, citric acid, and an acidic salt of any of the foregoing.

85. A method according to claim 75 wherein the at least one pharmaceutically acceptable organic acid is selected from malonic acid, succinic acid, fumaric acid, maleic acid, adipic acid, lactic acid, levulinic acid, sorbic acid, tartaric acid, maleic acid, ascorbic acid, citric acid, and an acidic salt of any of the foregoing.

86. A method according to claim 13 wherein the at least one pharmaceutically acceptable organic acid is citric acid.

87. A method according to claim 71 wherein the at least one pharmaceutically acceptable organic acid is citric acid.

88. A method according to claim 75 wherein the at least one pharmaceutically acceptable organic acid is citric acid.

89. A method according to claim 88 wherein the citric acid is citric acid anhydrous.

90. A method according to claim 13 wherein the pharmaceutically acceptable soluble salt of amoxicillin is sodium amoxicillin.

91. A method according to claim 71 wherein the pharmaceutically acceptable soluble salt of amoxicillin is sodium amoxicillin.

92. A method according to claim 75 wherein the pharmaceutically acceptable soluble salt of amoxicillin is sodium amoxicillin.

93. A method according to claim 85 wherein the pharmaceutically acceptable soluble salt of amoxicillin is sodium amoxicillin.

94. A method according to claim 88 wherein the pharmaceutically acceptable soluble salt of amoxicillin is sodium amoxicillin.

95. A method according to claim 13 wherein the pharmaceutically acceptable soluble salt of amoxicillin is crystallized sodium amoxicillin.

96. A method according to claim 88 wherein the pharmaceutically acceptable soluble salt of amoxicillin is crystallized sodium amoxicillin.

97. A method according to claim 13 wherein the ratio of the amount of amoxicillin in the composition to the amount of potassium clavulanate (amoxicillin free acid equivalent to clavulanic acid equivalent) is from about 2:1 to about 20:1.

98. A method according to claim 13 wherein the ratio of the amount of amoxicillin in the composition to the amount of potassium clavulanate (amoxicillin free acid equivalent to clavulanic acid equivalent) is from about 12:1 to about 20:1.

99. A method according to claim 13 wherein the ratio of the amount of amoxicillin in the composition to the amount of potassium clavulanate (amoxicillin free acid equivalent to clavulanic acid equivalent) is from about 14:1 to about 16:1.

100. A method according to claim 71 wherein the ratio of the amount of amoxicillin in the composition to the amount of potassium clavulanate (amoxicillin free acid equivalent to clavulanic acid equivalent) is from about 14:1 to about 16:1.

101. A method according to claim 75 wherein the ratio of the amount of amoxicillin in the composition to the amount of potassium clavulanate (amoxicillin free acid equivalent to clavulanic acid equivalent) is from about 14:1 to about 16:1.

102. A method according to claim 88 wherein the ratio of the amount of amoxicillin in the composition to the amount of potassium clavulanate (amoxicillin free acid equivalent to clavulanic acid equivalent) is from about 14:1 to about 16:1.

103. A method according to claim 97 wherein the pharmaceutically acceptable soluble salt of amoxicillin is crystallized sodium amoxicillin and the at least one pharmaceutically acceptable organic acid is citric acid anhydrous.

104. A method according to claim 13 wherein all of the potassium clavulanate of the composition is present in the first release phase.

105. A method according to claim 84 wherein all of the potassium clavulanate of the composition is present in the first release phase.

106. A method according to claim 94 wherein all of the potassium clavulanate of the composition is present in the first release phase.

107. A method according to claim 13 wherein the first release phase comprises at least one pharmaceutically acceptable soluble salt of amoxicillin, amoxicillin trihydrate, or a mixture thereof.

108. A method according to claim 105 wherein the first release phase comprises at least one pharmaceutically acceptable soluble salt of amoxicillin, amoxicillin trihydrate, or a mixture thereof.

109. A method according to claim 13 wherein the amount of amoxicillin (amoxicillin free acid equivalent) in the composition is from about 700 mg to about 2600 mg.

110. A method according to claim 99 wherein the amount of amoxicillin (amoxicillin free acid equivalent) in the composition is from about 700 mg to about 2600 mg.

111. A method according to claim 13 wherein the amount of amoxicillin (amoxicillin free acid equivalent) in the composition is from about 700 mg to about 1300 mg.

112. A method according to claim 99 wherein the amount of amoxicillin (amoxicillin free acid equivalent) in the composition is from about 700 mg to about 1300 mg.

113. A method according to claim 106 wherein the amount of amoxicillin (amoxicillin free acid equivalent) in the composition is from about 700 mg to about 1300 mg.

114. A method according to claim 13 wherein the amount of amoxicillin (amoxicillin free acid equivalent) in the composition is from about 950 mg to about 1300 mg.

115. A method according to claim 102 wherein the amount of amoxicillin (amoxicillin free acid equivalent) in the composition is from about 950 mg to about 1300 mg.

116. A method according to claim 13 wherein the amount of amoxicillin (amoxicillin free acid equivalent) in the composition is from about 1400 mg to about 2600 mg.

117. A method according to claim 102 wherein the amount of amoxicillin (amoxicillin free acid equivalent) in the composition is from about 1400 mg to about 2600 mg.

118. A method according to claim 13 wherein the amount of amoxicillin (amoxicillin free acid equivalent) in the composition is from about 1900 mg to about 2600 mg.

119. A method according to claim 106 wherein the amount of amoxicillin (amoxicillin free acid equivalent) in the composition is from about 1900 mg to about 2600 mg.

120. A method according to claim 13 wherein the amount of amoxicillin (amoxicillin free acid equivalent) in the composition is about 1000 mg or about 2000 mg.

121. A method according to claim 108 wherein the amount of amoxicillin (amoxicillin free acid equivalent) in the composition is about 1000 mg or about 2000 mg.

122. A method according to claim 13 wherein the amount of amoxicillin (amoxicillin free acid equivalent) administered to the patient is about 2000 mg.

123. A method according to claim 13 wherein the amount of amoxicillin (amoxicillin free acid equivalent) in the second release phase is from about 60% to about 80% by weight of the second release phase.

124. A method according to claim 105 wherein the amount of amoxicillin (amoxicillin free acid equivalent) in the second release phase is from about 60% to about 80% by weight of the second release phase.

125. A method according to claim 119 wherein the amount of amoxicillin (amoxicillin free acid equivalent) in the second release phase is from about 60% to about 80% by weight of the second release phase.

126. A method according to claim 113 wherein the amount of amoxicillin (amoxicillin free acid equivalent) in the second release phase is from about 60% to about 80% by weight of the second release phase.

127. A method according to claim 13 wherein the amount of amoxicillin (amoxicillin free acid equivalent) in the first release phase is 563 mg +/- 5% and the amount of amoxicillin in the second release phase is 438 mg +/- 5%.

128. A method according to claim 88 wherein the amount of amoxicillin (amoxicillin free acid equivalent) in the first release phase is 563 mg +/- 5% and the amount of amoxicillin in the second release phase is 438 mg +/- 5%.

129. A method according to claim 103 wherein the amount of amoxicillin (amoxicillin free acid equivalent) in the first release phase is 563 mg +/- 5% and the amount of amoxicillin in the second release phase is 438 mg +/- 5%.

130. A method according to claim 106 wherein the amount of amoxicillin (amoxicillin free acid equivalent) in the first release phase is 563 mg +/- 5% and the amount of amoxicillin in the second release phase is 438 mg +/- 5%.

131. A method according to claim 13 wherein the composition is divided into multiple dosage units.

132. A method according to claim 110 wherein the composition is divided into multiple dosage units.

133. A method according to claim 116 wherein the composition is divided into multiple dosage units.

134. A method according to claim 131 wherein the amoxicillin is present in at least two of the multiple dosage units.

135. A method according to claim 110 wherein the amoxicillin is present in at least two of the multiple dosage units.

136. A method according to claim 117 wherein the amoxicillin is present in at least two of the multiple dosage units.

137. A method according to claim 134 wherein the first release phase is in at least one dosage unit and the second release phase is in at least one other dosage unit.

138. A method according to claim 106 wherein the first release phase is in at least one dosage unit and the second release phase is in at least one other dosage unit.

139. A method according to claim 117 wherein the first release phase is in at least one dosage unit and the second release phase is in at least one other dosage unit.

140. A method according to claim 125 wherein the first release phase is in at least one dosage unit and the second release phase is in at least one other dosage unit.

141. A method according to claim 13 wherein the composition is in the form of a compressed tablet.

142. A method according to claim 141 wherein the composition is in the form of a monolith tablet.

143 . A method according to claim 74 wherein the composition is in the form of a compressed tablet.

144 . A method according to claim 85 wherein the composition is in the form of a compressed tablet.

145 . A method according to claim 93 wherein the composition is in the form of a compressed tablet.

146. A method according to claim 145 wherein the composition is in the form of a monolith tablet.

147. A method according to claim 103 wherein the composition is in the form of a compressed tablet.

148. A method according to claim 115 wherein the composition is in the form of a compressed tablet.

149. A method according to claim 130 wherein the composition is in the form of a compressed tablet.

150. A method according to claim 141 wherein the compressed tablet comprises at least two layers.

151 . A method according to claim 144 wherein the compressed tablet comprises at least two layers.

152 . A method according to claim 147 wherein the compressed tablet comprises at least two layers.

153 . A method according to claim 143 wherein all of the first release phase is in a first layer and all of the second release phase is in a second layer.

154. A method according to claim 144 wherein all of the first release phase is in a first layer and all of the second release phase is in a second layer.

155. A method according to claim 145 wherein all of the first release phase is in a first layer and all of the second release phase is in a second layer.

156. A method according to claim 141 wherein the second release phase of the tablet further comprises at least one release retarding excipient which is selected from pH sensitive polymers, release-retarding polymers which exhibit swelling characteristics when in an aqueous environment, polymeric materials which exhibit gelling characteristics when in an aqueous environment, and polymeric materials which exhibit both swelling and gelling characteristics when in an aqueous environment.

157. A method according to claim 156 wherein the at least one release retarding gellable polymer is selected from methylcelluloses, carboxymethylcelluloses, low-molecular weight hydroxypropylmethylcelluloses, low-molecular weight polyvinylalcohols, polyoxyethyleneglycols, and noncross-linked polyvinylpyrrolidones.

158. A method according to claim 85 wherein the second release phase of the tablet further comprises at least one release retarding excipient which is selected from pH sensitive polymers, release-retarding polymers which exhibit swelling characteristics

when in an aqueous environment, polymeric materials which exhibit gelling characteristics when in an aqueous environment, and polymeric materials which exhibit both swelling and gelling characteristics when in an aqueous environment.

159. A method according to claim 93 wherein the second release phase of the tablet further comprises at least one release retarding excipient which is selected from pH sensitive polymers, release-retarding polymers which exhibit swelling characteristics when in an aqueous environment, polymeric materials which exhibit gelling characteristics when in an aqueous environment, and polymeric materials which exhibit both swelling and gelling characteristics when in an aqueous environment.

160. A method according to claim 103 wherein the second release phase of the tablet further comprises at least one release retarding excipient which is selected from pH sensitive polymers, release-retarding polymers which exhibit swelling characteristics when in an aqueous environment, polymeric materials which exhibit gelling characteristics when in an aqueous environment, and polymeric materials which exhibit both swelling and gelling characteristics when in an aqueous environment.

161. A method according to claim 156 wherein the at least one release retarding excipient is xanthan gum.

162. A method according to claim 158 wherein the at least one release retarding excipient is xanthan gum.

163. A method according to claim 159 wherein the at least one release retarding excipient is xanthan gum.

164. A method according to claim 160 wherein the at least one release retarding excipient is xanthan gum.

165. A method according to claim 161 wherein the xanthan gum is present in an amount from about 0.5% to about 8% by weight of the second release phase.

166. A method according to claim 163 wherein the xanthan gum is present in an amount from about 0.5% to about 8% by weight of the second release phase.

167. A method according to claim 161 wherein the xanthan gum is pharmaceutical grade xanthan gum, 200 mesh.

168. A method according to claim 163 wherein the xanthan gum is pharmaceutical grade xanthan gum, 200 mesh.

169. A method according to claim 165 wherein the xanthan gum is pharmaceutical grade xanthan gum, 200 mesh.

170. A method according to claim 13 wherein the pharmaceutically acceptable soluble salt of amoxicillin and the at least one pharmaceutically acceptable organic acid are admixed in intimate contact such that upon exposure to an aqueous environment they interact such that rate of release of amoxicillin from the solid form of the second release phase is reduced compared to the rate of release of amoxicillin from the solid form of the first release phase.

171. A method according to claim 94 wherein the sodium amoxicillin and the at least one pharmaceutically acceptable organic acid are admixed in intimate contact such that upon exposure to an aqueous environment they interact such that rate of release of amoxicillin from the solid form of the second release phase is reduced compared to the rate of release of amoxicillin from the solid form of the first release phase.

172. A method according to claim 103 wherein the crystallized sodium amoxicillin and the citric acid anhydrous are admixed in intimate contact such that upon exposure to an aqueous environment they interact such that rate of release of amoxicillin from the solid form of the second release phase is reduced compared to the rate of release of amoxicillin from the solid form of the first release phase.

173. A method according to claim 13 wherein the composition has an in vitro dissolution profile such that about 45% to about 65% of the total amoxicillin is dissolved

within 30 minutes, as determined by the <711> Dissolution Test, Apparatus 2, provided in USP 23, 1995, in 900 mL of deionized water, at a paddle speed of 75 rpm.

174. A method according to claim 103 wherein the composition has an in vitro dissolution profile such that about 45% to about 65% of the total amoxicillin is dissolved within 30 minutes, as determined by the <711> Dissolution Test, Apparatus 2, provided in USP 23, 1995, in 900 mL of deionized water, at a paddle speed of 75 rpm.

175. A method according to claim 13 wherein the composition has an in vitro dissolution profile such that about 50% to about 75% of the total amoxicillin is dissolved within 60 minutes, as determined by the <711> Dissolution Test, Apparatus 2, provided in USP 23, 1995, in 900 mL of deionized water, at a paddle speed of 75 rpm.

176. A method according to claim 13 wherein the composition has an in vitro dissolution profile such that about 55% to about 85% of the total amoxicillin is dissolved within 120 minutes, as determined by the <711> Dissolution Test, Apparatus 2, provided in USP 23, 1995, in 900 mL of deionized water, at a paddle speed of 75 rpm.

177. A method according to claim 13 wherein the composition has an in vitro dissolution profile such that about 70% to about 95% of the total amoxicillin is dissolved within 180 minutes, as determined by the <711> Dissolution Test, Apparatus 2, provided in USP 23, 1995, in 900 mL of deionized water, at a paddle speed of 75 rpm.

178. A method according to claim 13 wherein the composition has an in vitro dissolution profile such that about 70% to about 100% of the total amoxicillin is dissolved within 240 minutes, as determined by the <711> Dissolution Test, Apparatus 2, provided in USP 23, 1995, in 900 mL of deionized water, at a paddle speed of 75 rpm.

179. A method according to claim 122 wherein the composition provides a mean maximum plasma concentration (C_{max}) of amoxicillin of at least 12 ug/mL.

180. A method according to claim 122 wherein the composition provides a mean maximum plasma concentration (C_{max}) of amoxicillin of at least 16 ug/mL.

181. A method according to claim 122 wherein the composition provides a mean plasma concentration of amoxicillin of at least 4 ug/mL for at least 4.4 hours.

182. A method according to claim 179 wherein the composition provides a mean plasma concentration of amoxicillin of at least 4 ug/mL for at least 4.4 hours.

183. A method according to claim 122 wherein the composition provides a mean plasma concentration of amoxicillin of at least 4 ug/mL for at least 4.8 hours.

184. A method according to claim 183 wherein the composition provides a mean maximum plasma concentration (C_{max}) of amoxicillin of at least 16 ug/mL.

185. A method according to claim 122 wherein the area under the curve (AUC) of the total amount of amoxicillin in the composition is at least 80% of that of the corresponding dosage of amoxicillin taken as a immediate release formulation, over the same dosage period.

186. A method according to claim 122 wherein the area under the curve (AUC) of the total amount of amoxicillin in the composition is at least 90% of that of the corresponding dosage of amoxicillin taken as a immediate release formulation, over the same dosage period.

187. A method according to claim 122 where the area under the curve (AUC) of the total amount of amoxicillin in the composition is at least 100% of that of the corresponding dosage of amoxicillin taken as a immediate release formulation, over the same dosage period.

188. A method according to claim 122 where the area under the curve (AUC) of the total amount of amoxicillin in the composition is at least 110% of that of the corresponding dosage of amoxicillin taken as a immediate release formulation, over the same dosage period.

189. A method according to claim 122 where the area under the curve (AUC) of the total amount of amoxicillin in the composition is at least 120% of that of the corresponding dosage of amoxicillin taken as a immediate release formulation, over the same dosage period.

190. A method according to claim 122 wherein the composition has an AUC, Cmax, and Tmax substantially according to Figure 5, profile A (Formulation VI).

191. A method according to claim 122 wherein the composition has an AUC, Cmax, and T>MIC substantially according to Figure 5, profile A (Formulation VI).

192. A method according to claim 122 wherein the composition has an AUC, Cmax, and Tmax substantially according to Figure 5, profile B (Formulation VII).

193. A method according to claim 122 wherein the composition has an AUC, Cmax, and T>MIC substantially according to Figure 5, profile B (Formulation VII).

194. A method according to claim 13 wherein the ratio of amoxicillin free acid equivalent to organic acid equivalent in the second phase is about 1:1.

195. A method according to claim 71 wherein the ratio of amoxicillin (amoxicillin free acid equivalent) in the first release phase to amoxicillin (amoxicillin free acid equivalent) in the second release phase is about 9:7.

196. A method according to claim 194 wherein the ratio of amoxicillin (amoxicillin free acid equivalent) in the first release phase to amoxicillin (amoxicillin free acid equivalent) in the second release phase is about 9:7.

197. A method according to claim 86 wherein the citric acid is citric acid anhydrous.

198. A method according to claim 89 wherein the pharmaceutically acceptable soluble salt of amoxicillin is crystallized sodium amoxicillin.

199. A method according to claim 122 wherein the amount of amoxicillin (amoxicillin free acid equivalent) administered is at a dosage regimen interval of about 12 hours.

200. A method according to claim 13 wherein the composition is administered at a dosage regimen interval of about 12 hours.

201. A method according to claim 109 wherein the amount of amoxicillin (amoxicillin free acid equivalent) administered is at a dosage regimen interval of about 12 hours.

202. A method according to claim 111 wherein the amount of amoxicillin (amoxicillin free acid equivalent) administered is at a dosage regimen interval of about 12 hours.

203. A method according to claim 114 wherein the amount of amoxicillin (amoxicillin free acid equivalent) administered is at a dosage regimen interval of about 12 hours.

204. A method for treating a bacterial infection in a patient, the method comprising administering to the patient in need thereof a therapeutically effective amount of a composition in solid dosage form comprising amoxicillin and potassium clavulanate in a weight ratio of amoxicillin to potassium clavulanate from about 2:1 to 20:1, the amount of amoxicillin is in the range of about 1950 to 2550mg; and the dosage regimen interval is about 12 hours,

such that the amount of amoxicillin released over thirty minutes is in the range about 45 to about 65% of the total amoxicillin content, over sixty minutes is in the range about 50 to about 75% of the total amoxicillin content, over two hours is in the range about 55 % to about 85% of the total amoxicillin content, over 180 minutes is in the range about 70 % to 95% of the total amoxicillin content and over 240 minutes is in the range about 70 to about 100% of the total amoxicillin content, as tested by the USP Dissolution Test, Apparatus 2, method at 37 degrees C, a paddle speed of 75 rpm and in 900 ml deionized water, over a period of 8 hours;

chosen such that the mean maximum plasma concentration (Cmax) is at least 12 micrograms/ml and the mean time the plasma concentration exceeds 4 micrograms/ml is at least 4.4 hours, when tested in a group of at least 7 healthy humans, based on blood sampling at half hourly intervals for the first two hours and thereafter at hourly intervals (at the start of a light meal and after an overnight fast).